Claims

1. Use of an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof for the treatment and/or prophylaxis of an inflammatory and/or immune-mediated disorder.

2. Use of an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof for the treatment and/or prophylaxis of an immune-mediated disorder.

3. Use of an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof for the treatment and/or prophylaxis of an autoimmune disease.

4. Use as claimed in claims 1 to 3 wherein the agent comprises adenylate CyaA or derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

5. Use as claimed in any of claims 1 to 4 wherein the adenylate cyclase toxin (CyaA) is combined with self or foreign antigens or fragments or mutants or variants or peptides thereof.

6. Use as claimed in claim 5 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

7. Use as claimed in claim 6 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney of graft recipient and neural graft components.

8. Use as claimed in any of claims 5 to 7 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

9. Use as claimed in claim 8 wherein the myelin protein is myelin basic protein or peptides thereof.

10. Use as claimed in claims 9 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein (MOG) synthetic peptide or fragment or mutant or variant thereof.

11. Use as claimed in claim 10 wherein the myelin basic protein is MOG peptide (35-55).

12. Use as claimed in any of claims 1 to 11 wherein the adenylate cyclase toxin (CyaA) is derived from *Bordetella pertussis, Bordetella bronchisepetica* or *Bordetella parapertussis* or related molecules from other bacteria.

13. Use as claimed in any of claims 1 to 12 wherein the agent modulates inflammatory cytokine production.

14. Use as claimed in any preceding claim wherein the immunomodulatory effects of CyaA on cells of the innate immune system is dependent on co-activation with a Toll-like receptor ligand.

15. Use as claimed in claim 14 wherein the Toll-like receptor ligand is LPS or another toll-like receptor ligand, selected from any one or more of CpG motifs, dsRNA, Poly (I:C) and the lipopeptide Pam3Cys.

16. Use as claimed in any preceding claim wherein CyaA promotes IL-10 and IL-6 production by macrophages and dendritic cells.

17. Use as claimed in any preceding claim wherein CyaA synergises with LPS to promote IL-10 and IL-6 production by macrophages and dendritic cells.

18. Use as claimed in any preceding claim wherein CyaA inhibits inflammatory cytokines, chemokines or other inflammatory mediators.

19. Use as claimed in claim 18 wherein the inflammatory cytokine is selected from any one or more of IL-12 or TNF-α, IFN-γ, IL-1, IL-23 and IL-27.

20. Use as claimed in claim 18 wherein the inflammatory chemokine is macrophage inflammatory protein-1α or macrophage inflammatory protein-1β.

21. Use as claimed in any preceding claim wherein CyaA promotes dendritic cell maturation following co-activation with TLR-ligands.

22. Use as claimed in claim 21 wherein CyaA promotes CD80 expression by dendritic cells.

23. Use as claimed in any preceding claim wherein CyaA inhibits TLR-ligand-induced dendritic cell activation.

24. Use as claimed in claim 23 wherein CyaA inhibits CD40 and ICAM-1 expression.

25. Use as claimed in any preceding claim wherein CyaA acts as an adjuvant *in vivo* to promote the induction of Th2 or Tr cells to co-administered antigens.

26. Use as claimed in claim 25 wherein the co-administered antigens comprise self or foreign antigens.

27. Use as claimed in any preceding claim wherein CyaA acts as an adjuvant *in vivo* to promote IgG1 antibodies to co-administered antigens.

28. Use as claimed in claim 27 wherein the co-administered antigens comprise self or foreign antigens.

29. Use as claimed in any preceding claim wherein the CyaA is present in a non-palmitoylated or non-acylated form.

30. Use as claimed in any preceding claim wherein the CyaA is substantially endotoxin free.

31. Use as claimed in any preceding claim wherein the CyaA is in the form of an immunomodulator, adjuvant, immunotherapeutic or anti-inflammatory agent.

32. Use as claimed in any preceding claim wherein the agent modulates inflammatory cytokine production induced by infection or trauma.

33. Use as claimed in any preceding claim wherein the disorder is sepsis or acute inflammation induced by infection, trauma or injury.

34. Use as claimed in any preceding claim wherein the disorder is selected from any one or more of Crohn's disease, inflammatory bowel disease, multiple sclerosis, type 1 diabetes, rheumatoid arthritis and psoriasis.

35. Use as claimed in any preceding claim wherein the disorder is asthma or atopic disease.

36. Use as claimed in any preceding claim in wherein the agent is in a form for oral, intranasal, intravenous, intradermal, subcutaneous or intramuscular administration.

37. Use as claimed in any preceding claim comprising repeated administration of the agent.

38. A product comprising CyaA or derivative or mutant or fragment or variant or peptide thereof in combination with an antigen, where said antigen is selected from a self-antigen and a foreign antigen.

39. A product as claimed in claim 38 wherein the CyaA comprises a derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

40. A product as claimed in claim 38 or 39 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

41. A product as claimed in claim 40 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into

the heart, lung, liver, pancreas, kidney of graft recipients and neural graft components.

42. A product as claimed in any of claims 38 to 41 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

43. A product as claimed in claim 42 wherein the myelin protein is myelin basic protein or peptides thereof.

44. A product as claimed in claim 43 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein synthetic peptide.

45. A product as claimed in claim 44 wherein the myelin basic protein is a MOG peptide (35-55).

46. A pharmaceutical composition comprising CyaA or derivative or mutant or fragment or variant or peptide thereof.

47. A pharmaceutical composition comprising CyaA or derivative or mutant or fragment or variant or peptide thereof as adjuvant for immunization with a self or foreign antigen.

48. A pharmaceutical composition comprising CyaA or derivative or mutant or fragment or variant or peptide thereof in combination with an antigen, where said antigen is selected from a self-antigen and a foreign antigen.

49. A pharmaceutical composition as claimed in claims 46 to 48 wherein the CyaA comprises a derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

50. A pharmaceutical composition as claimed in claim 46 to 49 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

51. A pharmaceutical composition as claimed in claim 50 wherein the antigens involved in graft rejection include antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney for graft recipient and neural graft components.

52. A pharmaceutical composition as claimed in any of claims 46 to 51 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

53. A pharmaceutical composition as claimed in claim 52 wherein the myelin protein is myelin basic protein or peptides thereof.

54. A pharmaceutical composition as claimed in claim 53 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein synthetic peptide.

55. A pharmaceutical composition as claimed in claim 54 wherein the myelin basic protein is a MOG peptide (35-55).

56. A pharmaceutical composition comprising non-acylated CyaA or derivative or mutant or fragment or variant or peptide thereof.

57. An immunomodulator comprising adenylate cyclase toxin (CyaA).

58. A recombinant non-acylated CyaA having immunomodulatory effects.

59. A vaccine comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

60. A vaccine as claimed in claim 59 comprising CyaA or derivative or mutant or fragment or variant or peptide thereof and an antigen.

61. A vaccine as claimed in claim 60 wherein the CyaA and antigen are present in a by weight ratio range of 0.01:1 to 100:1.

62. A vaccine as claimed in claim 60 wherein the CyaA and antigen are present in a molar ratio of 1:10 to 10:1.

63. Antibodies to adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

64. An amino acid sequence selected from any one or more of SEQ ID No. 3 or 4.

65. A method for the treatment and/or prophylaxis of an inflammatory and/or immune-mediated disorder comprising the step of administering an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

66. A method for the treatment and/or prophylaxis of an immune-mediated disorder comprising the step of administering an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

67. A method for the treatment and/or prophylaxis of an autoimmune disease comprising the step of administering an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

68. A method as claimed in claims 65 to 67 wherein the agent comprises adenylate CyaA or derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

69. A method as claimed in any of claims 65 to 68 wherein the adenylate cyclase toxin (CyaA) is combined with self or foreign antigens or fragments or mutants or variants or peptides thereof.

70. A method as claimed in claim 69 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

71. A method as claimed in claim 70 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney of graft recipient and neural graft components.

72. A method as claimed in any of claims 69 to 71 wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

73. A method as claimed in claim 72 wherein the myelin protein is myelin basic protein or peptides thereof.

74. A method as claimed in claims 73 wherein the myelin basic protein is myelin oligodendrocyte glycoprotein (MOG) synthetic peptide or fragment or mutant or variant thereof.

75. A method as claimed in claim 74 wherein the myelin basic protein is MOG peptide (35-55).

76. A method as claimed in any of claims 65 to 75 wherein the adenylate cyclase toxin (CyaA) is derived from *Bordetella pertussis*, *Bordetella bronchisepetica* or *Bordetella parapertussis* or related molecules from other bacteria.

77. A method as claimed in any of claims 65 to 76 wherein the agent modulates inflammatory cytokine production.

78. A method as claimed in of claims 65 to 77 wherein the immunomodulatory effects of CyaA on cells of the innate immune system is dependent on co-activation with a Toll-like receptor ligand.

79. A method as claimed in claim 78 wherein the Toll-like receptor ligand is LPS or another toll-like receptor ligand, selected from any one or more of CpG motifs, dsRNA, Poly (I:C) and the lipopeptide Pam3Cys.

80. A method as claimed in any of claims 65 to 79 wherein CyaA promotes IL-10 and IL-6 production by macrophages and dendritic cells.

81. A method as claimed in any of claims 65 to 80 wherein CyaA synergises with LPS to promote IL-10 and IL-6 production by macrophages and dendritic cells.

82. A method as claimed in any of claims 65 to 81 wherein CyaA inhibits inflammatory cytokines, chemokines or other inflammatory mediators.

83. A method as claimed in claim 82 wherein the inflammatory cytokine is selected from any one or more of IL-12 or TNF-α, IFN-γ, IL-1, IL-23 and IL-27.

84. A method as claimed in claim 82 wherein the inflammatory chemokine is macrophage inflammatory protein-1α or macrophage inflammatory protein-1β.

85. A method as claimed in any of claims 65 to 84 wherein CyaA promotes dendritic cell maturation following co-activation with TLR-ligands.

86. A method as claimed in claim 85 wherein CyaA promotes CD80 expression by dendritic cells.

87. A method as claimed in any of claims 65 to 86 wherein CyaA inhibits TLR-ligand-induced dendritic cell activation.

88. A method as claimed in claim 87 wherein CyaA inhibits CD40 and ICAM-1 expression.

89. A method as claimed in any of claims 65 to 88 wherein CyaA acts as an adjuvant *in vivo* to promote the induction of Th2 or Tr cells to co-administered antigens.

90. A method as claimed in claim 89 wherein the co-administered antigens comprise self or foreign antigens.

91. A method as claimed in any of claims 65 to 90 wherein CyaA acts as an adjuvant *in vivo* to promote IgG1 antibodies to co-administered antigens.

92. A method as claimed in claim 91 wherein the co-administered antigens comprise self or foreign antigens.

93. A method as claimed in any of claims 65 to 92 wherein the CyaA is present in a non-palmitoylated or non-acylated form.

94. A method as claimed in any of claims 65 to 93 wherein the CyaA is substantially endotoxin free.

95. A method as claimed in any of claims 65 to 94 wherein the CyaA is in the form of an immunomodulator, adjuvant, immunotherapeutic or anti-inflammatory agent.

96. A method as claimed in any of claims 65 to 95 wherein the agent modulates inflammatory cytokine production induced by infection or trauma.

97. A method as claimed in any of claims 65 to 96 wherein the disorder is sepsis or acute inflammation induced by infection, trauma or injury.

98. A method as claimed in any of claims 65 to 97 wherein the disorder is selected from any one or more of Crohn's disease, inflammatory bowel disease, multiple sclerosis, type 1 diabetes, rheumatoid arthritis and psoriasis.

99. A method as claimed in any of claims 65 to 98 wherein the disorder is asthma or atopic disease.

100. A method as claimed in any of claims 65 to 99 in wherein the agent is in a form for oral, intranasal, intravenous, intradermal, subcutaneous or intramuscular administration.

101. A method as claimed in any of claims 65 to 100 comprising repeated administration of the agent.